REMARKS/ARGUMENTS

The claims are 1-23. Claims 1 and 13 have been amended to better define the invention. Support for the claims may be found, *inter alia*, in the disclosure at page 11, second full paragraph, and at pages 15-16. Reconsideration is expressly requested.

Claims 1, 2, 4, 7-9, 11-16 and 19-20 were rejected under 35 U.S.C. 102(b) as being anticipated by *Pfeiffer et al. U.S. Patent No. 6,223,069*. The remaining claims 3, 5, 6, 10, 17-18 and 21-23 were rejected under 35 U.S.C. 103(a) as being unpatentable over *Pfeiffer et al.* in view of *Boas U.S. Patent No. 6,516,214*. Essentially the Examiner's position was that *Pfeiffer et al.* discloses the device and method recited in the claims except with regard to the steps of using a threshold value, extrapolation of a scaled inflow function, and applying a locally increased contact pressure, which were said to be shown by *Boas*.

This rejection is respectfully traversed.

As set forth in claims 1 and 13 as amended, Applicants' invention provides a device and a method, respectively, for measuring blood flow in an organ using an injected indicator. As recited in claim 1 as amended, the device includes a radiation source for emitting near infrared radiation into tissue of the organ at a first location, a sensor for detecting a proportion of the emitted near infrared radiation that exits from the organ at a second location, and an evaluation unit that detects the proportion of the emitted near infrared radiation that exits from tissue of the organ as an input signal. The input signal contains a pulsatile component and a non-pulsatile component, and the evaluation unit is programmed to perform the following evaluation steps:

(a) dividing up the input signal into the pulsatile component and the non-pulsatile component;

(b) determination of injected indicator concentration with reference to the organ tissue from the non-pulsatile component of the input signal;

(c) iterative determination of an inflow function i(t) that

characterizes blood flow through the organ by incrementally varying a mean transit time mtt until a stop criterion is reached;

(d) determination of injected indicator concentration with reference to blood volume in the organ from the pulsatile component of the input signal and the iteratively determined inflow function i(t);

(e) calculation of blood volume in the organ as a quotient of the injected indicator concentration with reference to the organ tissue and the injected indicator concentration with reference to the blood volume in the organ; and

(f) calculation of the blood flow in the organ as a quotient of the blood volume in the organ and the mean transit time mtt when the stop criterion has been reached.

These steps (a)-(f) are also recited in claim 13 as amended.

The amendments to claims 1 and 13 make clear that a pulsatile and non-pulsatile component are actually retrieved from the signal containing these components and that varying the mean transit time is part of the computerized iteration, i.e. a variable representing mean transit time is varied in the process of interation (rather than measuring varying permeation rates which would lead to varying mean transit times.)

With Applicants' invention, as recited in claims 1 and 13 as amended, separate calculations are performed with the pulastile and non-pulsatile component, respectively, of the input signal (optical density over time). In particular, according to the method and device recited in Applicants' claims 1 and 13 as amended.

Injected indicator concentration with reference to the organ tissue is determined using the non-pulsatile component of the input signal;

Injected indicated concentration with reference to blood volume in the organ is determined using the pulsatile component of the input signal.

The result is a calculated arterial inflow function of the observed optical segment.

None of the cited references discloses or suggests the method and device as recited in claims 1 and 13 as amended or the determining of an injected indicator concentration with reference to an organ tissue from a non-pulsatile component of an input signal alone. The references also fail to teach the benefits that result from the separate calculations performed with the pulsatile and non-pulsatile components respectively.

The primary reference to *Pfeiffer et al.* neither discloses nor suggests determining an injected indicator concentration with reference to an organ tissue from a non-pulsatile component (of an input signal) *alone*. In particular, *Pfeiffer et al.* fails to disclose or suggest even dividing up of an input signal into a pulsatile component and a non-pulsatile component *at all*. In contrast to Applicants' invention as recited in claims 1 and 13 as amended, wherein a calculated arterial inflow function of the observed optical segment results, *Pfeiffer et al.* uses an arterial dye curve observed via a pulse densitometry at the finger (as FIG. 1b shows).

As *Pfeiffer et al.* fails to disclose performing any separate calculations with a pulsatile and a non-pulsatile component respectively, *a fortiori Pfeiffer et al.* fails to disclose or even remotely suggest specifically calculating *indicator concentration with reference to the organ tissue from the non-pulsatile component* or *injected indicator comcentration with reference to the blood volume in the organ from a pulsatile component.*

In addition, Applicants wish to emphasize that *Pfeiffer et al.* fails also to disclose or suggest (either explicitly or implicitly) calculating the blood volume in an organ as a quotient of the injected indicator concentraton with reference to the organ tissue and the injected indicator concentration with reference to the blood volume in the organ.

Further, *Pfeiffer et al.* fails to disclose or suggest determination of an inflow function i(t) *by incrementally varying a mean transit time mtt until a stop criterion is reached.* In this connection, it is respectfully submitted that the Examiner's argument in the sentence bridging pages 2 and 3 of the Office Action appears not to be germane. The cited passage column 5,

lines 40-49 in *Pfeiffer et al.* merely mentions that blood flows through intra vascular compartments at varying rates, i.e. blood flow may be different at different locations. In contrast, Applicants' invention as recited in claims 1 and 13 as amended provides that in the process of calculation (a variable representing) mean transit time is varied in increments until a stop criterion is reached. In other words, the iteration is performed by varying (a variable representing) mean transit time.

Although *Pfeiffer et al.* does disclose that the transport function g(t) may be determined interatively by the least square method varying parameters of the transport function, nowhere does *Pfeiffer et al.* disclose or suggest determining an inflow function that characterizes blood flow through the organ by incrementally varying the mean transit time mtt until a stop criterion is reached. Instead, *Pfeiffer et al.* uses an inflow function required by pulse densitometry.

The defects and deficiencies of the primary reference to *Pfeiffer et al.* are nowhere remedied by the secondary reference to *Boas*. *Boas* discloses a method of detecting an ischemic event in a brain in a subject which includes establishing a reference

and the injected indicator concentration with reference to the blood volume in the organ.

Accordingly, it is respectfully submitted that the claims are patentable over the cited references.

In summary, claims 1 and 13 have been amended. In view of the foregoing, it is respectfully requested that the claims be allowed and that this application be passed to issue.

Respectfully submitted,
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I hereby certify that this correspondence is being deposited with the U.S. Postal Service as first class mail in an envelope addressed to: Commissioner of Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on March 29, 2007.

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